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EXAMINER	
SIMS, JASON M	

ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/057,270	FOX ET AL.	
	Examiner	Art Unit	
	JASON M. SIMS	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-10,19,21,23-30,32-34 and 36-38* is/are pending in the application.

4a) Of the above claim(s) *30,32-34 and 36-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-10,19,21 and 23-29* is/are rejected.

7)☒ Claim(s) *30, 32-34, and 36-38* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/15/2008 has been entered.

Claims 30, 32-34, and 36-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventive group, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/14/2007.

Applicant's arguments, filed 6/30/2008, have been fully considered. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Applicants have amended their claims, filed 6/30/2008, and therefore rejections newly made in the instant office action have been necessitated by amendment.

Claims 4-10, 19, 21, 23-24, and 26-29 are the current claims hereby under examination.

Claim Objections

The objections to claims 4 and 26-39 have been withdrawn because of applicant's amendments to the claims.

The following is a newly applied objection:

Claims 30, 32-34, and 36-38 are objected to because of the following informalities: The said claims have an inappropriate status identifier which should state "withdrawn." Appropriate correction is required.

Claim Rejections - 35 USC § 112

Response to Arguments:

Applicant's arguments, filed 8/32/2007, with respect to the rejection under 35 USC 112 second paragraph have been fully considered and are persuasive because of applicant's amendment. Therefore the rejection has been withdrawn.

The following rejections have been necessitated by amendment:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-10, 19, 21, 23-24, and 26-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 (and all claims dependent therefrom), step A, comprises a step of "obtaining or creating a database of nucleic acid sequences of a homologous target RNA or DNA, from all organisms or viruses," which has been deemed as vague and indefinite. It is unclear as to how this target RNA or DNA is chosen or to what exactly may comprise the "homologous target." Furthermore, it is unclear as to the criteria used for selecting the target RNA or DNA from a sample that may comprise viruses,

bacteria, mammalian tissue, etc. It appears from the claim wording that one target is selected, but unclear as to how that target is selected across varied organisms and viruses, etc. to ensure homology that can result in a database of nucleic acid sequences. Clarification via clearer claim wording is required.

Claim 4 (and all claims dependent therefrom) step C recites the limitation "each particular RNA or DNA subsequence of length n" in lines 1-2 of step C. There is insufficient antecedent basis for this limitation in the claim. It is unclear as to what subsequences said claim wording refers. Claim 4, step A, discloses obtaining target RNA or DNA from organisms or viruses, but does not disclose generating or creating any subsequences. Therefore, it is unclear as to what subsequences the wording in claim 4, step C refers.

Claim 4 (and all claims dependent therefrom), step C has been deemed as vague and indefinite. It is unclear as how to obtain or what criteria is used for creating “each particular RNA or DNA subsequence of length N.” Furthermore, it appears that N may be of any length, whereas it is unclear as to how the frequency of one single nucleotide leads to a determination of how it is characteristic of each node in the phylogenetic tree. Clarification via clearer claim wording is required.

Claim 4 (and all claims dependent therefrom), step E has been deemed as vague and indefinite. It is unclear as to how the derived plurality of signature probes necessarily determines the genetic affinity of twice the number of organisms or viruses. It is unclear as to how many signature probes may be derived wherein a sample only comprised two organisms. For example, it appears that more than one signature probe

may be derived per one characteristic signature sequence. Therefore, it is unclear as to how using several signature probes necessarily determine the genetic affinity of twice the number of organisms or viruses as probes used, such as in the instant case if only two organisms are present. Clarification via clearer claim wording is required.

Claim 4 (and all claims dependent therefrom), step E comprises the wording "characteristic signature sequences," which has been deemed as vague and indefinite. It is unclear as to what comprises these sequences or from where they are derived. It appears that these sequences are or maybe derived from the sequences stored in the database of step A. Clarification via clearer claim wording is required.

Claim 10 (and all claims dependent therefrom), step A, comprises the term "substantially," which is vague and indefinite and is not defined by the method of step A. It is unclear as to what constitutes the term "substantially" and/or metes and bounds of said term. Therefore, one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. Clarification via clearer claim wording is required.

Claim 23 (and all claims dependent therefrom), line 2, comprises the term "substantially," which is vague and indefinite and is not defined by the steps of claim 23. It is unclear as to what constitutes the term "substantially" and/or metes and bounds of said term. Therefore, one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. Clarification via clearer claim wording is required.

Claim 25 (and all claims dependent therefrom), is being rejected because it comprises a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim), which is considered indefinite,

since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 26 recites the broad recitation wherein 15 sequences are used to determine the genetic affinity of at least 18 organisms, and the claim also recites the number of organisms or viruses whose genetic affinity might be determined is at least twice the number of probes, which is the narrower statement of the range/limitation.

Claim 26 (and all claims dependent therefrom), has been deemed as vague and indefinite. It is unclear as to how the failure to detect a particular sequence results in increased confidence with which the genetic affinity of an organism or virus is determined. Clarification via clearer claim wording is required.

Claim 27 (and all claims dependent therefrom), is being rejected because it comprises a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim), which is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent

protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 28 recites the broad recitation wherein more than one oligonucleotide or sequence is detected, and the claim also recites the number of organisms or viruses whose genetic affinity might be determined is at least twice the number of probes, which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 102-Maintained

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 4-7 are rejected under 35 U.S.C. 102(e) as being anticipated by Ebersole et al. (US P/N 6,797,817).

The claims are directed to a method for determining the genetic affinity of organisms or viruses in a test sample containing a nucleic acid comprising the steps of:

A) Obtaining or developing a bifurcating node phylogenetic tree that substantially reflects the genetic relationship between the organisms or viruses included in a database of sequences of the nucleic acid.

B) Identifying the extent to which each particular oligonucleotide or sequence of length N is characteristic of each node in the bifurcating node phylogenetic tree of genetic relationship.

C) Deriving a plurality of nucleic acid signature probes from a signature-database of signature sequences that are complementary to a portion of the nucleic acid sequence of the organism or virus such that the number of organisms or viruses whose genetic affinity might be determined is at least twice the number of probes used.

D) Hybridizing the signature probes to the nucleic acid obtained from the test sample under conditions where a detectable signal will be produced by signature probes that hybridize to the nucleic acid of the organism or virus.

E) Identifying signature probes which produce detectable signal.

F) Determining which nodes in the bifurcating node phylogenetic tree of genetic relationship produced detectable signal to identify the closest genetic relatives of the organism or virus in the test sample.

Ebersole et al. teaches at Col. 9, lines 35-45 that a phylogenetic Tree of Life was obtained and used for extracting sequences that represented the major microorganism domains, Bacteria and Archeae, which could be used as signature sequences for

obtaining signature probes for testing for the presence of dechlorinating bacteria, which reads on method steps A-C. Furthermore, Ebersole et al. teaches at col. 4, lines 55-67 and col. 5, lines 1-4, that sequence profiles, from which signature probes are derived, may be used to identify and subtype bacteria with similar metabolic pathways. Therefore, a signature probe may be used to identify a dechlorinated bacteria and/or bacteria with similar metabolic pathways, such as subspecies of decholorinates, which further reads on step C) Deriving a plurality of nucleic acid signature probes from a signature-database of signature sequences that are complementary to a portion of the nucleic acid sequence of the organism or virus such that the number of organisms or viruses whose genetic affinity might be determined is at least twice the number of probes used. Ebersole et al. further teaches at col. 4, lines 55-67 and col. 5, lines 1-4 that the use of particular sequences may be used to identify decholorinators as well as for genetic sub-typing of species, which further reads on method step B) Identifying the extent to which each particular oligonucleotide or sequence of length N is characterisitic of each node in the bifurcating node phylogenetic tree of genetic relationship. Ebersole et al. further teaches at col. 2, lines 51-65, the use of signature probes in hybridizing to identifying sequences such that a signal is detectable, which reads on step D) Hybridizing the signature probes to the nucleic acid obtained from the test sample under conditions where a detectable signal will be produced by signature probes that hybridize to the nucleic acid of the organism or virus. Ebersole et al. at col. 5, lines 34-39, col. 6, lines 31-34, col. 6, lines 58-67, and col. 7, lines 1-9 teaches using signature sequences for generating probes and defines the use of probes and hybridization as such that is

consistent in the art, which produce detectable signals, which reads on step E) Identifying signature probes which produce detectable signal. Ebersole et al. teaches at col. 8, lines 38-40 that the sequences are useful for the identification of new dechlorinating bacteria, as well as for sub-typing strains of Dehalococcoides ethenogenes. Furthermore, Ebersole et al. teaches at col. 9, lines 19-40 that sequences used for obtaining probes and closest or nearest organisms to these sequences were determined, which all read on step E) Determining which nodes in the bifurcating node phylogenetic tree of genetic relationship produced detectable signal to identify the closest genetic relatives of the organism or virus in the test sample.

Ebersole et al. teaches claim 5 at col. 2, lines 50-59 wherein rDNA are used for obtaining probes, which reads the use of DNA for comprising signature probes.

Ebersole et al. teaches claim 6 at col. 6, lines 58-67 wherein hybridization is taught with that which is consistent in the art wherein a hybridization step is done in solution, which reads on claim 6.

Ebersole et al. teaches claim 7 at col. 13, lines 25-30 wherein it is taught that probes which generate a detectable signal are used, which inherently reads on a probe wherein the detection step utilizes radioactive labels, chemiluminescence, and/or fluorescence.

Response to Arguments:

Applicant's arguments filed 6/30/2008 have been fully considered but they are not persuasive.

Applicant argues that Ebersole does not teach a method for analyzing what is in the sample, only whether or not a particular organism or type is present.

Applicant's argument is not found persuasive because Ebersole et al. teach at col. 8, lines 38-40 that the sequences are useful for the identification of new dechlorinating bacteria, as well as for sub-typing strains of Dehalococcoides ethenogenes, wherein the identification of new dechlorinating bacteria reads on analyzing what is in the sample and even if it has not been encountered previously, not just if an organism is present.

Applicant argues that by seeking to determine the presence of a specific group of organisms whose identity is known ahead of time, Ebersole teach away from the present invention.

Applicant's argument is not found persuasive as Ebersole teach that "those 16S DNA gene sequences that were identified to be similar to the dechlorinating bacteria, Dehalococcoides enthenogenes DHE-195 (GenBank Accession No. AF004928), were aligned with selected 16s rRNA sequences extracted from the Ribosomal Database Project (Michigan State University) that were a representation of the major microorganism domains, Bacteria and Archeae in the Universal Phylogenetic Tree of Life. The sequences were aligned using MegAlign in DNAstar, using the default software parameters. From this alignment probable region for signature sequences were mapped. Furthermore, Ebersole teach the sequences are useful for the identification of new dechlorinating bacteria as well and therefore are not just specific.

Applicant argues that Ebersole relies on the presence of a single sequence which must be completely complementary to the target, which teaches away by suggesting that one must have specific sequences for every target of interest.

Applicant's argument is not found persuasive because applicant's claimed invention is based on specificity as in step E. Claim 4, step E derives signature probes from signature sequences, which will only be complementary to the target nucleic acid of the organisms which comprise the signature sequence. Therefore, the target nucleic acid of the organisms must have the signature sequence present.

Applicant further argues that Ebersole teaches away because its very nature can only produce probes for specific groupings.

Applicant's argument is not found persuasive because it is not commensurate in scope with the claimed invention. Ebersole's invention can detect known bacteria and also unknown or new bacteria, which reads on the instant claims which do not necessitate organisms from different groups to be present but rather a method for determining the affinity of organisms that are present. Therefore, a method which identifies previously unknown dechlorinating bacteria, but determines they are indeed dechlorinating bacteria, inherently determines the genetic affinity of the detected organism.

Applicant argues that the present application teaches that other nucleic acids can be used.

Applicant's arguments are not found persuasive because they are not commensurate in scope with the claimed invention.

Applicant argues that Ebersole uses the Tree of Life, i.e. phylogenetic tree for a different purpose wherein the present invention uses the tree to define the signature properties of every oligonucleotide of interest.

Applicant's arguments are not found persuasive as Ebersole uses the Tree of Life to determine the signature properties of oligonucleotides from a dechlorinating bacteria species, wherein that specific bacteria was of interest.

Applicant argues that the instantly claimed invention relates the occurrence of each candidate signature to the various groupings in the tree. Applicant further argues that Step A recites a database which comprises the signature properties of large numbers of N-mers.

Applicant's arguments are not found persuasive because they are not commensurate in scope with the claimed invention. Applicant's claim 4 step A only recites a database of nucleic acid sequences of a target DNA from all organisms that will be incorporated into the analysis, wherein there is no limitation as to how large or consequently how small the number of organisms.

Applicant further argues that the retained signature sequences have values of Qs above some criterion.

Applicant's arguments are not found persuasive as they are not commensurate in scope with the rejected claims as there is no calculation of a value for Q in the claim 4.

Applicant argues that the instant invention teaches that such sequences can recognize, for example, three distinct organisms or various groupings rather than just one.

Applicant's arguments are not found persuasive because they are not commensurate in scope with the claimed invention. Applicant's invention does not necessitate the recognition of various groupings, but just organisms in the sample, some of which may be known and some of which may not be known. Therefore, Ebersole, who teach that their invention can recognize both known dechlorinating bacteria and new, unknown, dechlorinating bacteria reads on the broad and reasonable interpretation of the instantly claimed invention.

Applicant further argues that the instantly claimed invention includes probes that determine genetic affinity without prior knowledge of what organism is present in a test sample, whereas Ebersole teach that the probes used target one specific group of bacteria.

Applicant's arguments are not found persuasive as they are not commensurate in scope with the claimed invention. Ebersole does target specifically dechlorinating bacteria, but the probes used may also detect unknown dechlorinating bacteria, i.e. new dechlorinating bacteria. In the invention taught by Ebersole, if the signature sequence is present in the target nucleic acid sequences of the organisms present, the characteristic signature sequences will hybridize, which reads on step E. The instantly claimed invention does not necessitate using a sample wherein there is a threshold number of known and unknown organisms present.

Applicant further argues that the signature sequences used by Ebersole are different from the signature sequences used by the instantly claimed invention. Applicant further states that the instantly claimed invention uses signature sequences

that are informative about the genetic affinity of the organism or virus carrying the nucleic acid.

Applicant's argument is not found persuasive because the signature sequences used by Ebersole, if hybridized to a new bacteria, are informative about the genetic affinity of that bacteria to dechlorinating bacteria, which also inherently, because of the use of the Phylogenetic tree of life, is informative about the genetic affinity of that organism to other organisms.

Applicant argues that the examiner does not point to any part of Ebersole that may read on step F.

Applicant's arguments are not found persuasive because as stated in the Final Office action mailed out 4/30/2008 Ebersole et al. further teach at col. 2, lines 51-65, the use of signature probes in hybridizing to identifying sequences such that a signal is detectable, which reads on step D) Hybridizing the signature probes to the nucleic acid obtained from the test sample under conditions where a detectable signal will be produced by signature probes that hybridize to the nucleic acid of the organism or virus. Ebersole et al. at col. 5, lines 34-39, col. 6, lines 31-34, col. 6, lines 58-67, and col. 7, lines 1-9 teach using signature sequences for generating probes and defines the use of probes and hybridization as such that is consistent in the art, which produce detectable signals.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jason Sims, whose telephone number is (571)-272-7540.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Marjorie Moran can be reached via telephone (571)-272-0720.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the Central PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central PTO Fax Center number is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

// Jason Sims //

/Michael Borin/

Primary Examiner, Art Unit 1631